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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,077	03/12/2004	Ramachandra Reddy	VASG-P01-001	2078

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EXAMINER	
CHONG, KIMBERLY	
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1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,077	REDDY ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7-11,14,16,18-25,59,61,62 and 65-83* is/are pending in the application.

4a) Of the above claim(s) *18-25,61,62,65-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-11,14,16 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/15/2008 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 04/14/2008 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 01/16/2008 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 04/14/2008, claims 1, 5, 7-11, 14, 16, 18-25, 59, 61-62, and 65-83 are pending, claims 1, 5, 7-11, 14, 16 and 59 are currently under examination, claims 2-4, 6, 12-13, 15, 17, 26-29, 30-58, 60, 63-64 and 84-91 have been canceled and claims 18-25, 61-62, and 65-83 are withdrawn as being drawn to a non-elected invention.

New Claim and Rejections

The following newly applied rejections are necessitated by claim amendments filed 04/14/2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 7-11, 14, 16 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stephenson et al. (BMC Molecular Biology 2001, Vol. 2, No. 15, pages 1-9), Bennett et al. (The Journal of Biological Chemistry, 1994, Vol. 268, No. 19, pages 14211-14218), Taylor et al. (DDT 1999, Vol. 4, No. 12, pages 562-567), Baracchini et al. (US Patent 5,801,154) and Tang et al. (Nucleic Acids Research 1993, Vol. 21, No. 11, pages 2729-2735).

The claims are drawn to an isolated nucleic acid compound comprising a nucleotide sequence of between 20 and 25 nucleotides which is complementary to a region of an EphB4 transcript, wherein the EphB4 transcript has a nucleotide sequence set forth in SEQ ID NO: 392, wherein the nucleic acid compound comprises one or more modified backbone or base moiety and comprises at least one comprises at least one 2'-O-alkylated ribonucleotide, wherein the compound is single-stranded, a DNA

molecule, a RNA molecule or DNA strand and an RNA strand, wherein the compound has at least one internucleotide linkage and drawn to pharmaceutical composition comprising said nucleic acid compound and further drawn to the antisense compound comprising SEQ ID No. 231.

Stephenson et al. teach that upregulation of the expression of several members of the Eph family of receptor tyrosine kinases has been associated with cancer and implies an important function for these proteins in the development and/or function of the tumor cells (see page 5). Stephenson et al. has found that EphB4 is overexpressed in colon cancer and suggests targeted disruption of the EphB4 gene in colon cancer cells and testing the effect of this on ability of the tumor cells to grow may provide useful information for developing strategies for treatment of colon cancer (see page 7).

Bennett et al. teach cloning and characterization of the human EphB4 cDNA (recited as HTK) (see Figure 1). Bennett et al. teach the overexpression of Eph genes can induce tumorigenicity (se page 14211).

Taylor et al. teach that antisense oligonucleotides 7-30 nucleotides long can be synthesized to inhibit the expression of any protein provided the cDNA sequence is known. Taylor et al. also indicate that making and using such oligonucleotides are available to those of ordinary skill in the art, that it is common practice to chemically modify the such oligonucleotides to prolong their bioactivity, and also teach that with software analysis and high affinity oligonucleotides, one needs to screen only 3-6 oligonucleotides to find one that inhibits its target 66-95% (p. 565).

Baracchini et al. teach that antisense oligonucleotides can be used for research purposes, and also teach that preferred antisense oligonucleotides are modified in their sugar, backbone linkage and nucleobase composition and particularly teach preferred 2'-O-alkyl modifications (see column 6). Baracchini teaches that such modifications are desirable in antisense oligonucleotides because these modifications have desirable properties such as enhanced cellular uptake, enhanced affinity for nucleic acid targets and increased stability in the presence of nucleases. Baracchini et al provide specific embodiments of such modifications at columns 6-8 and in Example 1. These specific examples taught by Baracchini et al include the presently claimed phosphorothioate linkages, 2'-O-methoxyethyl sugars, 5-methylcytosine and chimeric oligonucleotides which comprise both DNA and RNA strands. Tables 1-4 show the successful design and use of modified oligonucleotides in cells in culture. Table 1 exemplifies the successful practice of general antisense design taught at columns 8-10. Column 4 teaches various carriers for antisense delivery. Baracchini et al. also teaches at column 8 that antisense oligonucleotides are preferably 8 to 30 nucleotides and that it is more preferable to make antisense oligonucleotides that are 12 to 25 nucleotides in length. Baracchini is considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligonucleotides to target any known gene.

Tang et al. teach the use of self-stabilized oligonucleotides that comprise double strands and teach this double stranded oligonucleotide is more resistant to nucleolytic degradation (see 2729 and table 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the cDNA sequence of Bennett et al. to generate antisense sequences as taught by Taylor et al. for inhibition of EphB4 expression, and further, it would have been obvious to one of ordinary skill in the art to incorporate modifications into said antisense oligonucleotides and create double stranded oligonucleotides as taught by Baracchini et al. and Tang et al.

One would have wanted to create an antisense compound targeted to an EphB4 gene for the purpose of studying EphB4 function and whether inhibition of expression from this gene would be useful in the treatment of colon cancer given Stephenson et al. teach EphB4 is overexpressed in colon cancer cells. One of ordinary skill in the art would have wanted to provide the antisense oligonucleotide with increased stability by incorporation of modified nucleotides as taught by Baracchini et al. and would have wanted to protect the antisense compound from nuclease degradation by making the antisense double stranded as taught by Tang et al.

One would have expected to be able to create an antisense oligonucleotide sequence targeted to an EphB4 gene given that Taylor teaches that with software analysis and high affinity oligonucleotides, one of skill needs to screen only a few oligonucleotides to find one that inhibits its target 66-95%, and since Baracchini et al. teach making modified antisense compounds targeted to distinct regions of a target gene, the steps of making any antisense oligonucleotide are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 112

The rejection of claims 5 and 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claim 5 and 14 depend from canceled claim 3 and therefore are indefinite because it is unclear what further limitations the claims would encompass.

Re: Claim Rejections - 35 USC § 102

The rejection of claims 1, 7-11, 16 and 59 under 35 U.S.C. 102(b) as being anticipated by Monia et al. (U.S. Patent Number 6,270,030) is withdrawn and thus response to Applicant's argument is moot.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
Art Unit 1635